



CDC plans for COVID-19 vaccine effectiveness evaluation post-authorization and post-licensure

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Need for post-authorization or post-licensure vaccine effectiveness (VE) estimates

- Real world protection may differ from efficacy under trial conditions
 - Timing and coverage of 2-dose regimens
 - Cold chain requirements may be difficult to implement
- Build on evidence from phase 3 clinical trials including VE for
 - Key subpopulations
 - Severe disease
 - SARS-CoV-2 infection and transmission
 - Duration of protection



VE policy priorities: Results of internal and external input

Immediate First 2-4 months	<ul style="list-style-type: none">• Does vaccine protect against symptomatic disease as expected?
Subsequent	<ul style="list-style-type: none">• VE against key outcomes<ul style="list-style-type: none">• Severe disease• Non-severe disease• SARS-CoV-2 infection and transmission• VE in key subpopulations<ul style="list-style-type: none">• Adults aged ≥ 65 years, including those in long-term care facilities (LTCF)• People with key underlying conditions (e.g., immunocompromised, obesity, diabetes)• Disproportionately affected racial/ethnic populations (Black, Latinx, Native American/Alaska Native)• VE for regimen-related questions<ul style="list-style-type: none">• Single dose and prolonged dosing intervals; Mixed dose schedules (>1 product)
Later stage	<ul style="list-style-type: none">• Viral evolution: Do genome changes threaten VE?• Duration of protection• Comparative VE: Is one product better than another?

Challenges for observational COVID-19 VE studies

- Decision to be vaccinated may correlate with risk of disease
- Prior infection may bias estimate
- Imperfect laboratory testing poses a risk of misclassification
- COVID-19 epidemiology is highly dynamic
- Multiple products are in use simultaneously



Currently planned COVID-19 VE assessments

VE priority	Prospective data collection	Electronic health record (EHR) and claims analyses (coordination across US government)
Immediate priority		
Does vaccine work as expected to prevent symptomatic disease?	Test-negative design case-control among healthcare personnel	
Subsequent priorities		
Older adults, including residents of long-term care facilities (LTCF)	Case-control among adults ≥ 65 years (COVID-NET linked to CMS); National Healthcare Safety Network	CMS cohort (FDA, CMS) EHR datasets (CDC, VA, FDA)
Infection and transmission	Prospective longitudinal cohorts, including among healthcare personnel & frontline workers; case-ascertained household cohorts for transmission	
Severe disease/hospitalization	Test-negative design (for adults and children); conventional case-control using hospitalized controls; screening method	EHR datasets (CDC, VA, FDA): Retrospective cohort or test-negative design
Non-severe disease	Test-negative design among outpatients	Potentially using EHR datasets
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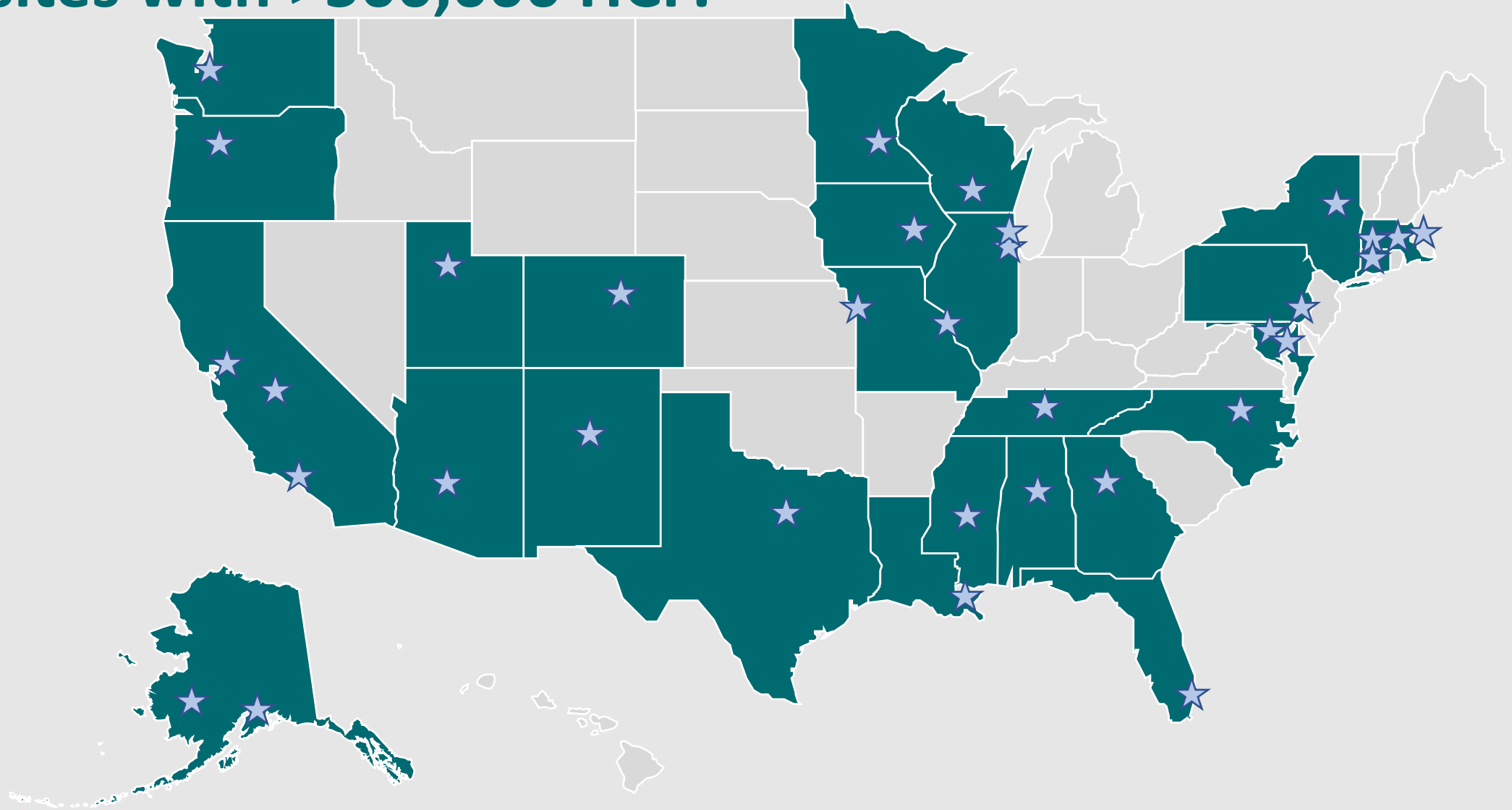


Assessing VE among healthcare personnel (HCP)

- Prospective test-negative design among HCP
 - Enroll HCP who are tested for COVID-19
 - Cases are test positive & controls are test negative
- Objectives:
 - Primary: evaluate VE of a complete schedule of COVID-19 vaccine against laboratory-confirmed symptomatic COVID-19 (by product if feasible)
 - Secondary will include VE by number of doses received, if feasible
- Timeline: January launch and enroll until sites have reached vaccine coverage >80% (2 doses)



VE assessment is being conducted across 26 states in 34 sites with >500,000 HCP.



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Assessing VE among adults aged ≥ 65 years

- CDC-led case-control assessment linking hospitalized cases from COVID-NET with CMS data
- FDA-led cohort analysis of CMS claims data
- Both will conduct separate analyses for adults ≥ 65 years who reside in
 - Community
 - Long-term care facilities (LTCF)



Assessing VE among residents of LTCF

- Data from the National Healthcare Safety Network (NHSN) LTCF surveillance and vaccine coverage modules
 - Weekly aggregate counts at the facility level of
 - New laboratory-confirmed COVID-19 cases
 - Vaccination status among all residents and among cases
 - Plan to calculate weekly attack rates among vaccinated and unvaccinated
- Data will be available starting early February
 - Initial analysis will require at least 8 weekly transmissions from LTCF with at least 50% vaccine coverage
 - Plans for ongoing analyses



Assessing vaccine impact in LTCF

- Ecologic analyses of vaccine coverage and COVID-19 disease rates among residents of LTCF
- Outbreak descriptive analyses before and after vaccine use



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Assessing VE against infection and transmission

- Leverage ongoing cohort of >5000 HCP and first-responders
 - Weekly testing for SARS-CoV-2 infection
 - Assessment of secondary transmission among household members
 - Cohort began in July 2020 and will continue through March 2022
- Working to expand case-ascertained household transmission studies to general population during widespread adult vaccination



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Assessing VE for disease severity and key populations

- Test-negative design and conventional case-control with hospitalized controls
 - Designed to assess severe disease/hospitalization and non-severe disease
 - Sites selected to include populations with underlying health conditions, racial/ethnic groups disproportionately affected by COVID-19, and American Indian/Alaska Native populations
- Screening method analyses
- EHR and claims-based assessments



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Assessing vaccine impact

- Ecologic analyses of the association of disease incidence and/or seroprevalence with vaccine coverage
- Comparisons of expected vaccine impact from models with actual observed impact



Assessing VE for regimen-related questions

- Single dose
- Prolonged dosing intervals (>3-4 weeks)
- Mixed dose schedules (>1 product)

- All platforms except NHSN will collect individual-level information on dose dates and type
- Best opportunity may come from large prospective, EHR, and claims assessments among the general adult population



Do viral genome changes threaten VE?

- Prospective platforms for general adult population will collect specimens from cases, where possible, for whole genome sequencing
 - Will not be performed in real time
 - May not be powered for variant-specific VE assessments
- A separate team in the vaccine evaluation unit is dedicated to assessing vaccine breakthrough cases
- Work is part of broader CDC efforts to monitor the impact of SARS-CoV-2 variants



Assessing VE among children and pregnant women

- Children
 - Planning a prospective test-negative design assessment to evaluate VE against COVID-19 hospitalizations
 - Leveraging an existing surveillance network of approximately 20-40 sites for pediatric COVID-19 hospitalizations and multisystem inflammatory syndrome in children (MIS-C)
 - EHR and claims database analyses will be used to estimate VE in children
- Pregnant women
 - Exploring EHR cohort and prospective case-control VE assessments



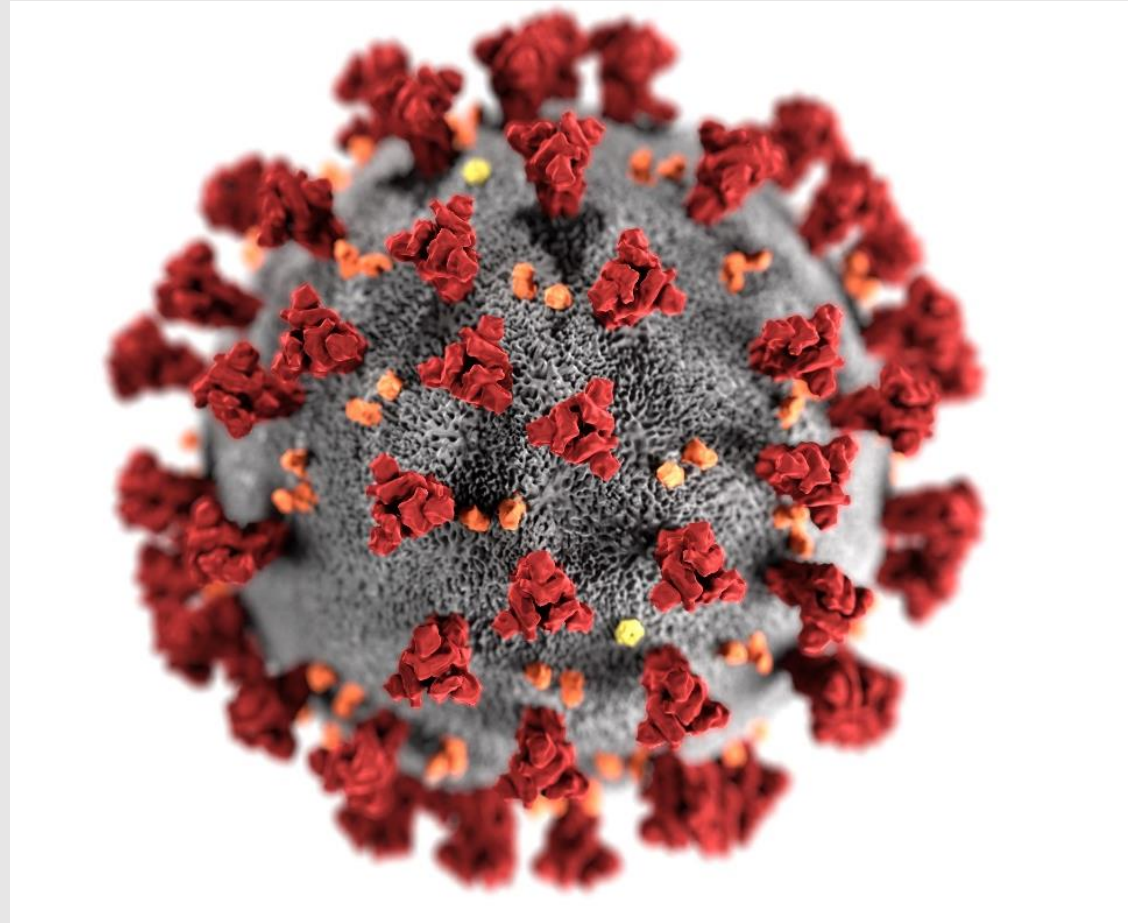
Conclusions

- Urgent need for VE data to guide vaccine policy
- VE portfolio leverages multiple platforms, data sources, and methods
- Early VE assessments will focus on healthcare personnel and residents of LTCF
- Portfolio will continue to evolve as more information from Phase 3 trials and real-world evidence become available



Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov



The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.